



Kaufman oculocerebrofacial syndrome

Kaufman oculocerebrofacial syndrome is a disorder characterized by eye problems (oculo-), intellectual disability (-cerebro-), and a distinctive pattern of facial features (-facial).

Most individuals with Kaufman oculocerebrofacial syndrome have an unusually small head size (microcephaly), and some have structural abnormalities of the brain. Affected individuals have weak muscle tone (hypotonia), and are delayed in developing motor skills such as walking. Intellectual disability is severe or profound. Most affected individuals never acquire the ability to speak.

Eye abnormalities and their effect on vision vary among people with Kaufman oculocerebrofacial syndrome. Some people with this disorder have abnormally small or poorly developed eyes (microphthalmia); microcornea, in which the clear front covering of the eye (cornea) is small and abnormally curved; missing pieces of tissue in structures that form the eye (coloboma); or underdevelopment of the nerves that carry signals between the eyes and the brain (optic nerve hypoplasia). Eyes that do not look in the same direction (strabismus), nearsightedness (myopia) or farsightedness (hyperopia), or an inward turning of the lower eyelid (entropion) can also occur.

Individuals with Kaufman oculocerebrofacial syndrome typically have a characteristic pattern of facial features. These include highly arched eyebrows, an increased distance between the inner corners of the eyes (telecanthus), a narrowing of the eye opening (blepharophimosis), skin folds covering the inner corner of the eyes (epicanthal folds), droopy eyelids (ptosis), and outside corners of the eyes that point upward (upslanting palpebral fissures). Ear abnormalities include low-set ears with small lobes and growths of skin (skin tags) in front of the ear (preauricular tags). The nose has a narrow bridge, a wide base, and nostrils that open to the front rather than downward (anteverted nares). Affected individuals may also have flat cheeks; a space between the nose and upper lip (philtrum) that is unusually long and smooth; a narrow mouth; and an unusually small jaw (micrognathia).

Other signs and symptoms that can occur in people with this disorder include short stature; hearing loss; and abnormalities of the heart, respiratory tract, gastrointestinal tract, kidneys, genitals, or skeleton. Affected individuals can live into adulthood; however, their average life expectancy is unknown because of the small number of people who have been diagnosed with this disorder.

Frequency

The prevalence of Kaufman oculocerebrofacial syndrome is unknown. At least 14 affected individuals have been described in the medical literature.

Genetic Changes

Kaufman oculocerebrofacial syndrome is caused by mutations in the *UBE3B* gene. This gene provides instructions for making a protein that plays a role in the ubiquitin-proteasome system, which is the cell machinery that breaks down (degrades) unwanted proteins. The specific proteins that the UBE3B protein helps break down are unknown, but research suggests that UBE3B functions in the nervous system, digestive tract, respiratory system, and other organs and tissues, from before birth into adulthood.

The *UBE3B* gene mutations that cause Kaufman oculocerebrofacial syndrome are thought to result in an abnormal UBE3B protein that cannot function properly or that is unstable and is rapidly broken down. Loss of this protein's function likely prevents cells from eliminating certain unnecessary proteins, resulting in problems with development and function of the brain, eyes, and other parts of the body.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- blepharophimosis-ptosis-intellectual disability syndrome
- BPIDS
- KOS
- oculocerebrofacial syndrome, Kaufman type

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Kaufman oculocerebrofacial syndrome
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1855663/>

Other Diagnosis and Management Resources

- GeneReview: Kaufman Oculocerebrofacial Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK390670>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Craniofacial Abnormalities
<https://medlineplus.gov/craniofacialabnormalities.html>
- Health Topic: Developmental Disabilities
<https://medlineplus.gov/developmentaldisabilities.html>
- Health Topic: Optic Nerve Disorders
<https://medlineplus.gov/opticnervedisorders.html>

Genetic and Rare Diseases Information Center

- Kaufman oculocerebrofacial syndrome
<https://rarediseases.info.nih.gov/diseases/3084/kaufman-oculocerebrofacial-syndrome>

Educational Resources

- Centers for Disease Control and Prevention (CDC): Intellectual Disability Fact Sheet
https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/intellectualdisability.pdf
- Disease InfoSearch: Kaufman oculocerebrofacial syndrome
<http://www.diseaseinfosearch.org/Kaufman+oculocerebrofacial+syndrome/3962>
- MalaCards: kaufman oculocerebrofacial syndrome
http://www.malacards.org/card/kaufman_oculocerebrofacial_syndrome
- Merck Manual Consumer Version: Intellectual Disability
<http://www.merckmanuals.com/home/children-s-health-issues/learning-and-developmental-disorders/intellectual-disability>

- Orphanet: Oculocerebrofacial syndrome, Kaufman type
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2707
- University of Arizona Database of Hereditary Ocular Disease
<http://disorders.eyes.arizona.edu/disorders/kaufman-oculocerebrofacial-syndrome>

Patient Support and Advocacy Resources

- The Arc: For People with Intellectual and Developmental Disabilities
<http://www.thearc.org/>
- University of Kansas Support Resources: Blind/Visual Impairment
<http://www.kumc.edu/gec/support/visual.html>

GeneReviews

- Kaufman Oculocerebrofacial Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK390670>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Kaufman+oculocerebrofacial+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

OMIM

- KAUFMAN OCULOCEREBROFACIAL SYNDROME
<http://omim.org/entry/244450>

Sources for This Summary

- Basel-Vanagaite L, Dallapiccola B, Ramirez-Solis R, Segref A, Thiele H, Edwards A, Arends MJ, Miró X, White JK, Désir J, Abramowicz M, Dentici ML, Lepri F, Hofmann K, Har-Zahav A, Ryder E, Karp NA, Estabel J, Gerdin AK, Podrini C, Ingham NJ, Altmüller J, Nürnberg G, Frommolt P, Abdelhak S, Pasmanik-Chor M, Konen O, Kelley RI, Shohat M, Nürnberg P, Flint J, Steel KP, Hoppe T, Kubisch C, Adams DJ, Borck G. Deficiency for the ubiquitin ligase UBE3B in a blepharophimosis-ptosis-intellectual-disability syndrome. *Am J Hum Genet.* 2012 Dec 7;91(6): 998-1010. doi: 10.1016/j.ajhg.2012.10.011.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23200864>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3516591/>
- Basel-Vanagaite L, Yilmaz R, Tang S, Reuter MS, Rahner N, Grange DK, Mortenson M, Koty P, Feenstra H, Farwell Gonzalez KD, Sticht H, Boddaert N, Désir J, Anyane-Yeboah K, Zweier C, Reis A, Kubisch C, Jewett T, Zeng W, Borck G. Expanding the clinical and mutational spectrum of Kaufman oculocerebrofacial syndrome with biallelic UBE3B mutations. *Hum Genet.* 2014 Jul; 133(7):939-49. doi: 10.1007/s00439-014-1436-2.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24615390>

- Flex E, Ciolfi A, Caputo V, Fodale V, Leoni C, Melis D, Bedeschi MF, Mazzanti L, Pizzuti A, Tartaglia M, Zampino G. Loss of function of the E3 ubiquitin-protein ligase UBE3B causes Kaufman oculocerebrofacial syndrome. J Med Genet. 2013 Aug;50(8):493-9. doi: 10.1136/jmedgenet-2012-101405.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23687348>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3717725/>
 - Pedurupillay CR, Barøy T, Holmgren A, Blomhoff A, Vigeland MD, Sheng Y, Frengen E, Strømme P, Misceo D. Kaufman oculocerebrofacial syndrome in sisters with novel compound heterozygous mutation in UBE3B. Am J Med Genet A. 2015 Mar;167A(3):657-63. doi: 10.1002/ajmg.a.36944.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/25691420>
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